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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,450	04/27/2001	William H. Frey II	83935	9084

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EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,450	FREY ET AL.	
	Examiner	Art Unit	
	Traviss C. McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-80* is/are pending in the application.

4a) Of the above claim(s) *5-31,34-36 and 45-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,32,33 and 37-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed February 10, 2005 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 1-2, 4, 34-35, and 44 have been amended.

Remarks drawn to rejections of Office Action mailed August 10, 2004 include:

Claim objections: which have been overcome by applicant's amendments and have been withdrawn.

112 1st paragraph rejection: which has been maintained ion part for reasons of record.

112 2nd paragraph rejection: which has been maintained for reasons of record.

103(a) rejection: which have been overcome by applicant's amendments and has been withdrawn.

An action on the merits of claims 1-4 and 32-44 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Election/Restrictions

Claims 34-36 are withdrawn from further consideration as these claims as amended no longer depend from any pending claims and only depend from withdrawn claims. Since claims 34-34 do not depend from claims which are currently under examination, these claims are being withdrawn from consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

Claims 1-3, 32-33, and 37-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

In the amendment filed by applicants on February 10, 2005, applicants have amended claim 1 from "small alkyl group" to "an alkyl group". Applicants do not have support for the claims as amended. The original disclosure does not provide any guidance for indicating that "small alkyl group" is anything other than methyl (see page 5, lines 3-11). The changing of the scope of a claim, either by broadening or narrowing, can be construed as new matter as either is capable of changing the scope of what is claimed, and the narrower or broader group must be supported in its entirety by the specification as originally filed. Applicants did not set forth a group represented by "alkyl", and this could include molecules which are hundreds of carbon atoms long, being either branched or linear. As set forth supra, the original disclosure does not have support for the compound as presently claimed, but only has support for methyl. Applicant is required to cancel the portion of the claims which states that the various R groups are "alkyl groups".

It is noted that a rejection of the claims is reviewable by the Board of Patent Appeals and Interferences.

The rejection of claims 1-4, 32-33 and 37-44 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of protecting the muscarinic acetylcholine receptor in Alzheimer's patients from inactivation caused by oxidative stress induced by heme/peroxide or the low molecular weight inhibitor found in Alzheimer's disease patients using compounds with 2-4 phosphorus atoms optionally in combination with other known antioxidants, does not reasonably provide enablement for methods of protecting the muscarinic acetylcholine receptor and an additional tissue component in Alzheimer's patients from anything using compounds with 2-4 phosphorus atoms, is maintained for reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims - The nature of the invention

Claim 1 of the instant application is drawn to a method of protecting the mAChR receptor in Alzheimer's patients from anything comprising administering a pyrophosphate analog with 2-4 phosphorus atoms. Dependent claims provide the method additionally protects a tissue component, wherein the tissue component can be receptors, proteins, lipids, nucleic acids, carbohydrates, hormones, vitamins, and cofactors. The receptors are the limited to be receptors for various things, such as for any neurotransmitter, any neuropeptide, any steroid, any purine, any ion channel, etc. Claim 4 is drawn to protecting any tissue in an Alzheimer's patient from oxidative stress by administering a pyrophosphate analog with 2-4 phosphorus atoms. Dependent claims 32-33 additionally limit the compound to be used to various compounds such as pyrophosphate, imidodiphosphate, etc., limits the patient to be treated to one who has various diseases, and provides methods for combination therapy with various substances. Dependent claims 37-43 provide for various combination therapies. Dependent claim 44 limits the compound to one that has 2-3 phosphorous molecules.

The state of the prior art

Antioxidants are known in the art to be chemical substances that neutralize the oxidant effects of free radicals and other substances. Compounds are known in the art to have varying degrees of antioxidant activity, as set forth by the differences of the 7-methoxychromones and 7-hydroxychromones (compound #556 and feruloyl aloesin) of Yu et al (US Patent 5,939,395). Antioxidants estrogen, vitamin E and vitamin C are known to have protected muscarinic

acetylcholine receptors (mAChR) from inhibition by the low molecular weight inhibitor found in Alzheimer's disease patients or hemin (Venters et al., Brain Research, 764, pp. 93-100, 1997). The art is silent to the correlation between inhibition of mAChR in Alzheimer's patients and protecting any other tissue component from anything.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the active agent of claim 1 has efficacy in Alzheimer's patients in protecting mAChR inactivation caused by oxidative stress induced by heme/peroxide or the endogenous low molecular weight inhibitor found in Alzheimer's patients, however the art is silent with regard to the predictability of the compound of claim 1 protecting the mAChR receptor from anything else, nor the compound of claim 1 protecting the various additional tissues components claimed.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claim as written. The examiner notes, there has not been provided sufficient instruction or sufficient methodological procedures to support the alleged efficacy instantly asserted using a compound from claim 1 and 4.

The existence of working examples

The working examples set forth in the instant specification are directed to the use of various compounds in testing for protection of mAChR from inactivation caused by the low molecular weight inhibitor found in Alzheimer's patients or heme/peroxide. It is noted that there

has been no combination therapy tested. There are no tests indicative of the additional tissue components being protected. The results showed that various compounds do protect a mAChR from the inhibitory effects of the endogenous LMW inhibitor and heme/peroxide, thus allowing agonist/antagonist binding to the mAChR. However, there has not been provided sufficient evidence which would warrant the skilled artisan to accept the data and information provided in the working examples as correlative proof that the compound of claim 1 would indeed protect the mAChR receptor from anything, nor that the compound of claim 1 would also protect the various tissue components of claims 2-3.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the use of the compound of claim 1 in a method of protecting the mAChR receptor in Alzheimer's patients from anything without undue experimentation. Additionally, the instant disclosure is not seen to enable the use of the compound of claim 4 in a method of protecting the any tissue in an Alzheimer's patient from anything without undue experimentation. Lastly, the instant specification is not seen to enable the use of the compound of claim 1 in a method of protecting the various tissue components in Alzheimer's patients from anything without undue experimentation. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation. One skilled in the art would be confronted with an undue burden of experimentation to isolate, characterize, and test the various compounds of claim 1 to determine if indeed they have efficacy as protective agents from any number of various possibilities in various tissue components. As set forth supra, applicants have

successfully shown methods of protecting the muscarinic acetylcholine receptor in Alzheimer's patients from inactivation caused by oxidative stress induced by heme/peroxide or the endogenous low molecular weight inhibitor found in Alzheimer's disease patients using compounds with 2-4 phosphorus atoms and optionally with other known antioxidants.

Applicants amended claims 1 and 4 to limit the compound used in the method to one of 2-4 phosphorous atoms and amended claim 1 to limit the tissue component which is to be protected to the mAChR receptor in Alzheimer's patients, however, applicant did not address the additional tissue components of claims 2-3 which are not deemed to be enabled, nor did applicants limit the tissue in claim 4 to the mAChR receptor in Alzheimer's patients.

The rejection of claims 1-4, 32-33 and 37-44 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained for reasons of record.

The term "a **small** alkyl group" in claim 1 is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. It is noted that applicants amended the phrase in line 7 and 13, but did not amend the phrase in line 5, for example. Moreover, the phrase "small alkyl group" is indefinite in every instance where the term "small" is not specifically

defined (i.e., claim 4), as one of skill in the art would not be appraised as to the meets and bounds of the claims.

Conclusion

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh
April 14, 2005

James O. Wilson
Supervisory Patent Examiner
Art Unit 1623